## (19) World Intellectual Property Organization

International Bureau



## 

(43) International Publication Date 6 May 2004 (06.05.2004)

**PCT** 

# (10) International Publication Number WO 2004/038404 A3

(51) International Patent Classification<sup>7</sup>: G01N 33/574, C12N 9/02

(21) International Application Number:

PCT/EP2003/011180

(22) International Filing Date: 8 October 2003 (08.10.2003)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data: 02079489.7

28 October 2002 (28.10.2002) EP

(71) Applicant (for all designated States except US): PHAR-MACIA ITALIA SPA [IT/IT]; Via Robert Koch, 1.2, I-20152 Milan (IT).

(72) Inventors; and

- (75) Inventors/Applicants (for US only): GERONI, Cristina [IT/IT]; Via Correggio, 48, I-20149 Milan (IT). PAC-CIARINI, Maria, Adele [IT/IT]; Via degli Imbriani, 39, I-20158 Milan (IT).
- (81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU,

CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

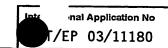
(84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

#### Published:

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments
- (88) Date of publication of the international search report: 17 June 2004

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.





A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 G01N33/574 C12N9/02

C. DOCUMENTS CONSIDERED TO BE RELEVANT

According to International Patent Classification (IPC) or to both national classification and IPC

#### **B. FIELDS SEARCHED**

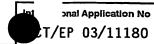
Minimum documentation searched (classification system followed by classification symbols) IPC 7 G01N C12N C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

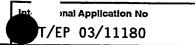
Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BIOSIS, EMBASE

Category °	Citation of document, with indication, where appropriate, of	the relevant passages	Relevant to claim No.
X	EP 1 088 900 A (EPIDAUROS BIO AG) 4 April 2001 (2001-04-04) paragraphs '0004!,'0005!,'00 claims 26-39		1,3,5,7, 9,10
X	of nemorubicin (methoxymorpholinyldoxorubicin PNU-152243A) and its 13-0H me (PNU-155051A) in human plasma J. PHARM. BIOMED. ANAL., vol. 30, 15 October 2002 (2002) pages 377-389, XP002274208	tabolite ."	1,2
Y	the whole document	-/	3–10
	ner documents are listed in the continuation of box C.	χ Patent family members are listed i	n annex.
'A' docume consider earlier of filing docume which citation other representations.	int which may throw doubts on priority claim(s) or is cited to establish the publication date of another n or other special reason (as specified) ant referring to an oral disclosure, use, exhibition or	<ul> <li>"T" later document published after the linte or priority date and not in conflict with cited to understand the principle or the invention</li> <li>"X" document of particular relevance; the cannot be considered novel or cannot involve an inventive step when the document of particular relevance; the cannot be considered to involve an involve and in the art.</li> <li>"&amp;" document member of the same patent in the art.</li> </ul>	the application but every underlying the laimed invention be considered to current is taken alone laimed invention rentive step when the re other such docu- is to a person skilled
	actual completion of the international search  9 March 2004	Date of mailing of the international sear	ch report
		Authorized officer	

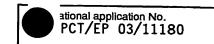


C/C	offen) DOCUMENTO CONTROL	T/EP 03/11180
C.(Continua Category °	Citation of document with indication, where acceptant	
Odlegory	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	RIVORY L.P. ET AL.: "Optimizing the Erythromycin Breath Test for use in cancer patients." CLIN. CANCER RES., vol. 6, September 2000 (2000-09), pages 3480-3485, XP002274209 cited in the application the whole document	1,3,5,7, 9,10
X	RIVORY L.P. ET AL.: "Hepatic cytochrome P450 3A drug metabolism is reduced in cancer patients who have an acute-phase response." BRIT. J. CANCER, vol. 87, 29 July 2002 (2002-07-29), pages 277-280, XP002274210 the whole document	1,3,5,7, 9,10
X	HIRTH J.A. ET AL.: "The effect of an individual's cytochrome CYP3A4 activity on docetaxel clearance." CLIN. CANCER RES., vol. 6, April 2000 (2000-04), pages 1255-1258, XP001121612 the whole document	1,3,5,7, 9,10
X	MARTINEZ C. ET AL.: "Expression of paclitaxel-inactivating CYP3A activity in human colorectal cancer: implications for drug therapy." BRIT. J. CANCER, vol. 87, 9 September 2002 (2002-09-09), pages 681-686, XP002274211 the whole document	1,3,5,7, 9,10
Y	QUINTIERI L. ET AL.: "In vivo antitumor activity and host toxicity of methoxymorpholinyl doxorubicin: role of cytochrome P450 3A." CANCER RES., vol. 60, 15 June 2000 (2000-06-15), pages 3232-3238, XP002274212 the whole document	1-10
Y	WO 01 58444 A (THE UNIVERSITY COURT OF THE UNIVERSITY OF ABERDEEN) 16 August 2001 (2001-08-16) page 5, line 5 -page 6, line 22 page 9, line 11 - line 21 claims 1-21	1-10



	tion) DOCUMENTS CONSIDERED TO BE RELEVANT	T/EP 03/11180
tegory °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 02 088714 A (MCGILL UNIVERSITY) 7 November 2002 (2002-11-07) page 63 -page 64 page 80 -page 86 page 188 -page 193 page 199 -page 202 claims 1-79	1-10





Box I	Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)
This Inte	emational Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
1. 🗶	Claims Nos.: 1-2, 5-8 because they relate to subject matter not required to be searched by this Authority, namely:  see FURTHER INFORMATION sheet PCT/ISA/210
2.	Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
з. 🗌	Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box II	Observations where unity of invention is lacking (Continuation of item 2 of first sheet)
This Inte	rnational Searching Authority found multiple inventions in this international application, as follows:
1.	As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2.	As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3.	As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4.	No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
Remark o	The additional search fees were accompanied by the applicant's protest.  No protest accompanied the payment of additional search fees.

International Application No. PCT/ EP 03 /11180

### FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.1

Although claims 1-2 and 5-8 are directed to a method of treatment of the human/animal body by surgery, the search has been carried out and based on the alleged effects of the compound/composition.

Continuation of Box I.1

Claims Nos.: 1-2, 5-8

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by surgery

Int∈	nal Application N		
	T/EP	03/11180	

Patent document cited in search report		Publication date		Patent family member(s)	Publication date
EP 1088900	Α	04-04-2001	EP	1088900 A1	04-04-2001
			AU	7001800 A	17-04-2001
			ΑU	7513300 A	17-04-2001
			CA	2379541 A1	22-03-2001
			CA	2381066 A1	22-03-2001
			WO	0120025 A2	22-03-2001
			WO	0120026 A2	22-03-2001
			ΕP	1210462 A2	05-06-2002
			EP	1210463 A2	05-06-2002
			JP	2003509063 T	11-03-2003
			JP	2003509064 T	11-03-2003
			NO	20021146 A	15-04-2002
			NO	20021147 A	03-05-2002
WO 0158444	Α	16-08-2001	AU	3206001 A	20-08-2001
			CA	2399402 A1	16-08-2001
			EP	1261332 A1	04-12-2002
			WO	0158444 A1	16-08-2001
			JP	2003522143 T	22-07-2003
			US	2003162727 A1	28-08-2003
WO 02088714	Α	07-11-2002	WO	02088714 A2	07-11-2002
			EP	1386156 A2	04-02-2004
			US	2003108484 A1	12-06-2003